



Five-year Results of a Randomised Clinical Trial of Endovenous Laser Ablation of the Great Saphenous Vein with and without Ligation of the Saphenofemoral Junction **CME**

B.C.V.M. Disselhoff ^{a,*}, D.J. der Kinderen ^b, J.C. Kelder ^c, F.L. Moll ^d

^a Department of Surgery, Bergmankliniek, Bilthoven, The Netherlands

^b Department of Dermatology, Dermalink, Amersfoort, The Netherlands

^c Department of Cardiology, St Antonius Hospital, Nieuwegein, The Netherlands

^d Division of Vascular Surgery, University Medical Centre Utrecht, Utrecht, The Netherlands

Submitted 26 September 2010; accepted 9 December 2010

Available online 18 February 2011

KEYWORDS

Endovenous laser ablation;
Great saphenous vein;
Saphenofemoral ligation;
Recurrent varicose veins

Abstract *Objective:* To evaluate whether ligation of the saphenofemoral junction (SFL) improves the results of endovenous laser ablation (EVLA) of the great saphenous vein (GSV) in a 5-year randomised clinical trial (RCT).

Methods: Forty-three symptomatic patients (86 limbs) with bilateral incompetent GSVs were randomised so that one limb underwent EVLA without SFL and the other limb underwent EVLA with SFL. Eleven patients were lost to follow-up and two patients died, leaving 30 patients (60 limbs) for analysis. Duplex-confirmed groin varicose vein recurrence and venous clinical severity score (VCSS) were investigated at 6, 12, 24 and 60 months after treatment.

Results: Five-year life table analysis showed freedom from groin varicose vein recurrence in 79% of limbs (95% confidence interval (CI); 67–92%) in the EVLA without SFL group and in 65% of limbs (95% CI; 51–82) in the EVLA with SFL group ($P = 0.36$). Groin varicose vein recurrence was due to neo-vascularisation (0%), re-canalisation (9%) and incompetent tributaries in 14% in the EVLA without SFL group, and to neo-vascularisation (33%), re-canalisation (0%) and incompetent tributaries (0%) in the EVLA with SFL group. The VCSS improved significantly and was comparable in both groups. *Conclusion:* The rate of varicose vein recurrence was similar in both study groups. There was less neo-vascularisation in the EVLA without SFL group, but more incompetent tributaries and early re-canalisation at 5-year follow-up than in the EVLA with SFL group.

Registration number: ISRCTN60300873 (<http://www.clinical-trials.com>).

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* Corresponding author. Dr. B.C.V.M. Disselhoff, Burgemeester s' Jacoblaan 56, 1401 BS Bussum, The Netherlands. Tel.: +31 302953737.
E-mail address: disselhoff@ziggo.nl (B.C.V.M. Disselhoff).

Introduction

Endovenous laser ablation (EVLA) is used to treat varicose veins due to reflux in the great saphenous vein (GSV) and is usually performed without ligation of the saphenofemoral junction (SFL).¹ Critics of endovenous techniques in the treatment of varicose veins dispute the wisdom of not ligating the saphenofemoral junction (SFJ) because of failure of vein occlusion due to the large diameter of the saphenous vein, the development of a deep vein thrombosis (DVT) or a pulmonary embolism. In addition, groin tributaries may remain patent, which might promote recurrence of varicose veins. Others argue that avoiding surgical disruption of the SFJ, as occurs during ligation, may actually reduce neo-vascularisation, leading to a reduced rate of recurrence.² According to van Rij et al., neo-vascularisation is a major cause of duplex-confirmed recurrence of reflux in the groin after adequate surgery.³

A randomised clinical trial (RCT) was conducted to determine whether SFL improves the results of EVLA of the GSV. In our initial report, we found no clear advantage for additional SFL in terms of occlusion rate, venous clinical severity score (VCSS)⁴ and duplex-confirmed recurrent varicose veins, at 2 years' follow-up.⁵ However, there is a tendency that with longer follow-up the incidence of duplex-confirmed neo-vascularisation in the groin following EVLA without SFL is reduced and may also result in lower recurrence rates.^{6,7}

The aim of this study was to evaluate the 5-year results of the single-centre RCT comparing EVLA of the GSV with and without SFL in patients with primary bilateral varicose veins.

Patients and Methods

Data were collected in a single-centre RCT of consecutive patients with primary bilateral varicose veins, referred to our hospital between March 2003 and February 2005. The study protocol was approved by the regional ethics committee of the Mesos Medical Centre, Utrecht, The Netherlands.

A detailed description of the perioperative details and assessments has been published in our initial report.⁵ Several important aspects of this study deserve mention here. The inclusion criteria were patients with primary symptomatic varicose veins, CEAP (Clinical, Etiologic, Anatomic and Pathophysiologic) clinical class C2 venous disease,⁸ informed written consent, age range 20–75 years and GSV incompetence from the groin to below the knee, defined as retrograde flow lasting longer than 0.5 s on duplex ultrasound scanning (ATL 3500 HDI, ATL Ultrasound, Bothell, WA, USA). Reflux was detected by applying compression to the calf followed by sudden release, using rapid inflation pneumatic cuffs (Hokanson, Bellevue, USA). Tributaries at the SFL (external pudendal, superficial epigastric and superficial circumflex iliac vein) and accessory saphenous veins exhibiting bi-directional flow were defined as incompetent. Reasons for exclusion were previous venous surgery, a history of suspected or proven DVT, CEAP clinical class C3–6 venous disease, deep venous reflux, incompetence of the perforating veins below the knee, reflux of the GSV just to the knee, duplication of the GSV, withholding of patient consent and others (Fig. 1). After patients had given written informed consent, they

were randomised using numbered and sealed envelopes so that one limb underwent EVLA without SFL and the other limb underwent EVLA with SFL.

The procedures were performed as day cases. All patients underwent their assigned treatment. Thirty-five patients (81%) preferred general or spinal anaesthesia over local anaesthesia. One surgeon experienced in EVLA techniques and varicose vein surgery performed all the procedures. The EVLA procedure has been described elsewhere.⁵ In brief, the GSV, 5 cm below the knee, was accessed under ultrasound guidance and the tip of the laser fibre was positioned 0.5–1 cm below the SFJ. Under ultrasound monitoring, 250 ml of tumescent local anaesthetic was administered within the fascial sheath of the GSV. For patients undergoing treatment under spinal or general anaesthesia, 250 ml NaCl 0.9% was infiltrated around the vein. Manual compression was applied over the GSV, while 12-W intermittent (one pulse on, one pulse off) or 14-W continuous laser energy was delivered from 0.5 to 1 cm below the SFJ to the access site at a pullback rate of 0.2 cm s⁻¹. High ligation was performed through a 4-cm incision in the groin, with flush division of the GSV and division of all tributaries beyond the second level of division. The groin incision was closed with the tissue adhesive Dermabond® (Johnson & Johnson, NJ, USA). After the procedure, a graduated, thigh-length compression stocking (20–30 mmHg) was worn day and night for 1 week. Post-operative pain was managed with aceclofenac, 100 mg twice daily for 1 week. Patients were instructed to walk immediately after the procedure, and were encouraged to resume normal activities and return to work as soon as possible.

At each visit, physicians assessed patients' signs and symptoms using the VCSS, and employed duplex ultrasound imaging to assess the abolition of GSV reflux and the presence of recurrent varicose veins. Abolition of GSV reflux was demonstrated by its complete occlusion or obliteration, and duplex-ultrasound-detected recurrent varicose veins were classified in accordance with Stonebridge.⁹ At 6 weeks, residual varicosities and accessory saphenous veins underwent sclerotherapy with Aethoxysclerol 1% (Kreussler, Germany). These adjunctive procedures were intended as part of the initial treatment approach, with the intention of removing all varicosities. The primary outcome measure was freedom from recurrent varicose veins in the groin, as confirmed by duplex ultrasound, 5 years after treatment. Secondary outcomes were abolition of reflux in the GSV, VCSS scores and freedom from overall recurrent varicose veins. Follow-up at 6, 12, 24 and 60 months was complete for 86 limbs (100%), 82 limbs (95%), 78 limbs (91%) and 60 limbs (70%), respectively. Two patients were lost to follow-up at 12 months because of discomfort during duplex examination, two at 24 months because of pregnancy and nine at 5 years (five did not attend, two died (myocardial infarction and carcinoma), and two refused).

Statistical Analysis

We hypothesised that SFL would not improve the outcome of EVLA. To our knowledge in 2003, there were no RCT data available comparing different options for venous surgery in the same patient with primary varicose veins. Hence, a formal power calculation could not be performed. The

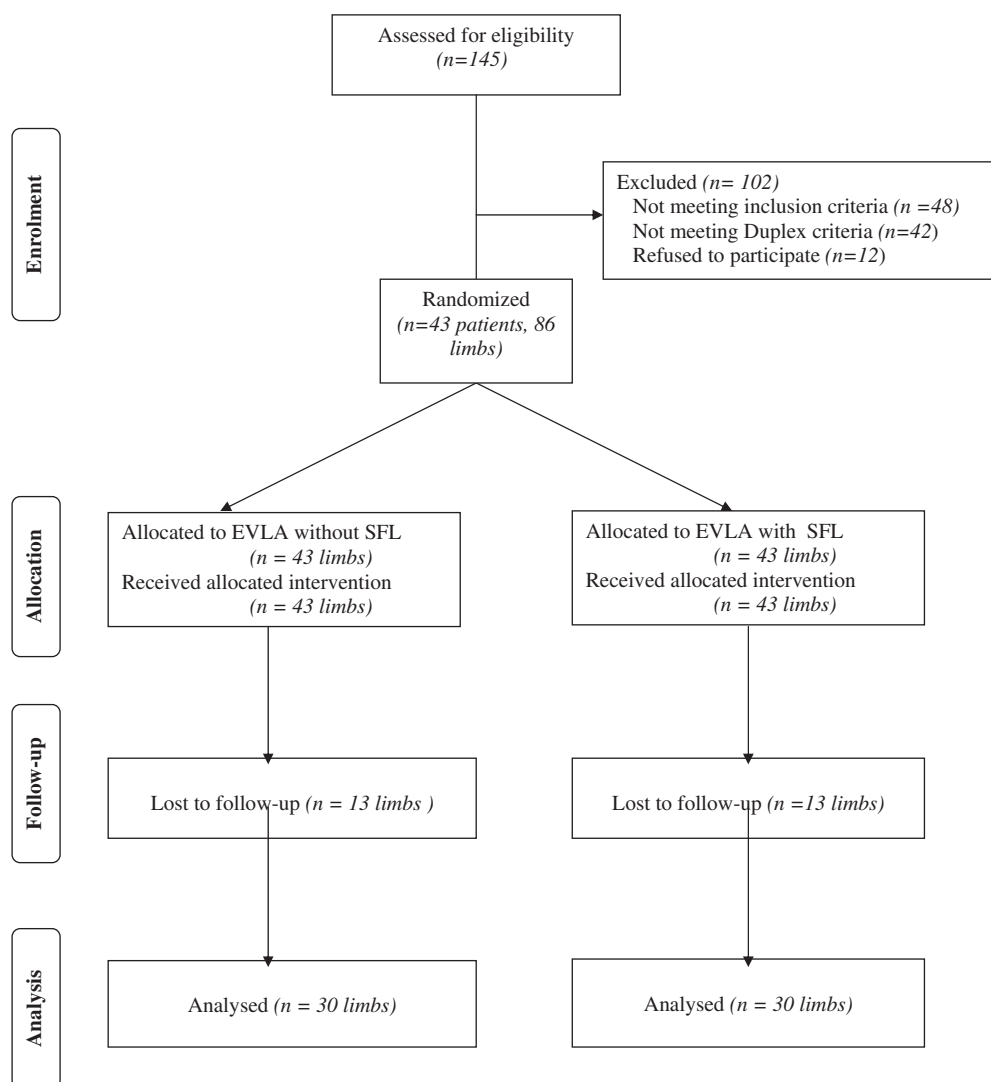


Figure 1 CONSORT flow chart. EVLA, endovenous laser ablation. SFL, saphenofemoral ligation.

precision of a trial with 43 as the denominator will yield a standard error of 5.7% (pertaining to a proportion of 85%). Analysis of the outcome was on an intention-to-treat basis. Data from the assessments were coded, and analyses were performed using R (version 2.10 for Windows; www.r-project.org) and Microsoft Excel (Microsoft Redmond, Washington, USA). The difference in primary outcome for EVLA without ligation versus EVLA with ligation was assessed by freedom from duplex-detected recurrence, graphically depicted by means of Kaplan–Meier curves, assuming that the event took place exactly halfway between two follow-up visits and difference assessed by means of the log-rank test. Generalised linear mixed-effects modelling was used to compare scores for VCSS over time, also taking into account the paired nature of the randomisation of the limbs. $P < 0.05$ was considered to indicate a statistically significant difference.

Results

A detailed description of the 2-year results has been published in our initial report.⁵ Of 145 patients assessed for the trial, 43 (30%) agreed to randomisation (Fig. 1). The median age of the

patients was 45 years (range 23–74 years). Thirty-six patients (84%) were female and 27 (63%) had a body mass index less than 25 kg m^{-2} . Base line characteristics of the GSV in the two groups were not statistically significant. Incompetent tributaries at the SFJ were detected in 2 (2.5%) of 79 visible tributaries in the EVLA without SFL group and in 4 (4.8%) of 84 visible tributaries in the EVLA with SFL group. There was no significant difference between the groups concerning the amount of laser energy delivery ($58.6 \text{ J (cm vein)}^{-1}$ (S.D. 12.2) in the EVLA without SFJ ligation group and $58.9 \text{ J (cm vein)}^{-1}$ (S.D. 12.0) in the EVLA with SFJ ligation group). At 6 weeks, residual non-GSV varicose veins were detected in 10 limbs (23%) in the EVLA with SFL group and in eight limbs (18.6%) in the EVLA without SFL group. Accessory saphenous veins were still visible in six limbs in each group. In accordance with the protocol, all these patients requested and underwent sclerotherapy with Aethoxysclerol 1%.

Primary Outcome

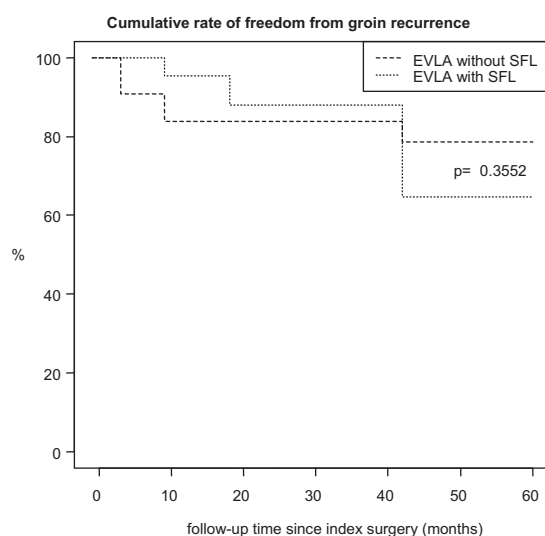
The results of the duplex ultrasound imaging are shown in Table 1. Five-year life table analysis (Fig. 2) showed

Table 1 Recurrent varicose veins demonstrated at Duplex ultrasound and scores for VCCS.

	Baseline	6 Month (n = 43)	1 Year (n = 41)	2 Year (n = 39)	5 Year (n = 30)
Type 1a recurrence					
EVLA without SFL		4	0	0	0
EVLA with SFL		0	0	0	0
Type 1b recurrence					
EVLA without SFL		0	3	0	3
EVLA with SFL		0	0	0	0
Type 1c recurrence					
EVLA without SFL		0	0	0	0
EVLA with SFL		0	2	3	9
Type 2a recurrence					
EVLA without SFL		0	0	0	0
EVLA with SFL		0	0	0	0
Type 2b recurrence					
EVLA without SFL		0	0	3	1
EVLA with SFL		1	1	3	2
SSV recurrence					
EVLA without SFL		0	1	1	0
EVLA with SFL		0	0	1	0
No recurrence					
EVLA without SFL		39	35	31	27
EVLA with SFL		42	39	32	21
VCSS ^a					
EVLA without SFL	3.1 (1–5)	1.0 (0–4)	0.5 (0–2)	0.5 (0–2)	0.6 (0–2)
EVLA with SFL	3.1 (1–5)	0.9 (0–3)	0.5 (0–2)	0.5 (0–2)	0.9 (0–3)

Type 1a: incompetent great saphenous vein (GSV). Type 1b: incompetent tributaries. Type 1c: neovascularization (defined as serpentine tributaries arising from the ligated SFJ). Type 2a: cross-groin connections. Type 2b: thigh perforators. EVLA, endovenous laser ablation. VCCS, venous clinical severity score. SFL, saphenofemoral ligation. SSV, small saphenous vein.

^a Values are mean (range).



No (of limbs) at risk

EVLA without SFL	43	39	34	32	20
EVLA with SFL	43	43	39	34	16

Figure 2 Kaplan–Meier life table analysis of freedom from duplex-confirmed groin (Type 1a, 1b and 1c) varicose vein recurrence. EVLA, endovenous laser ablation. SFL, saphenofemoral ligation.

freedom from groin (type 1a, 1b and 1c) varicose vein recurrence in 79% of limbs (95% confidence interval (CI); 67–92%) in the EVLA without SFL group and in 65% of limbs (95% CI; 51–82) of limbs in the EVLA with SFL group ($P = 0.36$). Groin varicose vein recurrence was due to neovascularisation (without SFL: 0%, with SFL: 33%), re-canalisation (without SFL: 9%, with SFL: 0%) and incompetent tributaries (without SFL: 14%, with SFL: 0%). The VCCS improved significantly and was comparable in both groups.

Secondary Outcomes

In the EVLA without SFL group, 38 (88%) treated GSV segments were ablated completely, and in the EVLA with SFL group, 42 (98%) treated GSV segments. The differences between the two groups were not statistically significant. Although continuous exposure resulted in abolition of the GSV reflux in more limbs than did intermittent exposure (98% (45/46) vs. 88% (35/40), respectively), the differences between the two groups were not statistically significant. In the EVLA without SFL group, four limbs had type 1a varicose vein recurrence and no improvement in VCCS scores, requiring additional SFJ ligation at the 6-month follow-up. At the 12-, 24- and 60-month follow-ups, re-canalisation of the GSV was not observed in either group.

VCCS scores improved significantly in both groups, but the differences between the groups were not significant (Table 1).

Five-year life table analysis (Fig. 3) showed overall freedom from varicose vein recurrence (type 1a, 1b, 1c, 2a and 2b and small saphenous vein) in 69% of limbs (95% CI; 56–84%) in the EVLA without SFL group and in 51% of limbs (95% CI; 37–69%) of limbs in the EVLA with SFL group ($P = 0.25$).

Discussion

Together with the previous 2-year observation,⁵ this study has shown no advantage for additional SFL, as assessed by duplex-confirmed recurrence of varicose veins and VCSS scores at 5 years' follow-up. Furthermore, there appears less neo-vascularisation after EVLA without SFL, but more early re-canalisation and incompetent tributaries.

Endovenous procedures are performed without ligation of the SFJ and tributaries. Surgical ligation of the SFJ is considered to be a major reason for groin recurrence after high ligation and stripping. According to van Rij et al.,³ the rate of groin recurrence after adequate surgery is 23% of which neo-vascularisation accounts for 85%. The notion that neo-vascularisation in the groin after surgical treatment leads to recurrence is supported by histological evidence. Glass¹⁰ described healing angiogenesis induced by the groin wound as a major source of new channels reconnecting superficial veins to the deep femoral vein around a ligated SFJ. Our study demonstrated neo-vascularisation in 14 limbs (33%) after EVLA with SFL and in 0 limbs after EVLA without SFL, at 5-year follow-up. In their prospective cohort study comparing surgery and EVLA, Theivacumar et al.,⁶ detected neo-vascularisation in 11 of 60 limbs (18%) in the surgical group and in 1 of 69 limbs (1%) in the EVLA group, at 2 years'

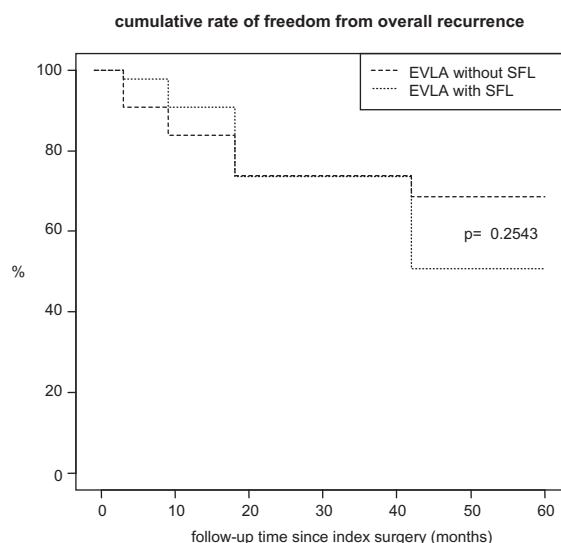
follow-up. These two studies, and the 5-year results of an RCT comparing endovenous laser and surgery for great saphenous varicose veins⁷ appear to show less neo-vascularisation after EVLA without SFL. To minimise the risk of neo-vascularisation, we now avoid the use of SFL.

In the EVLA without SFJ ligation group, 16 limbs were treated with less than $50 \text{ J (cm vein)}^{-1}$, of which four limbs developed re-canalisation. As described in our initial report, successful GSV ablation depends not only on the mode and amount of laser energy delivered, laser wavelength and pullback rate, but also on methodological aspects, such as the use of perivenous infiltration, manual compression over the vein during the procedure and a fibre tip position 0.5–1 cm below the SFJ. Failure to occlude the proximal GSV and/or early re-canalisation is reported in fewer than 10% of veins after EVLA.¹¹ It seems likely that these patients represent primary treatment failures due to the method of laser energy delivery. It is also possible that these veins had temporarily occluded, but underwent early thrombus dissolution and/or had insufficient thermal injury to the endothelial layer of the treated vein. Further re-canalisation of the GSV did not occur during follow-up, a finding confirmed by others.^{12,13}

Groin recurrence due to incompetent tributaries, such as the anterior accessory saphenous vein, occurred in six limbs (14%) after EVLA without SFL but in none after EVLA with SFL. Reflux in tributaries such as the anterior accessory saphenous vein is an important cause of recurrence.¹⁴ In this study, we found that of 206 (80%) visible SFL tributaries at preoperative duplex scanning, 18 (9%) had reflux in one or more SFL tributaries; these were treated with sclerotherapy 6 weeks after EVLA. Competent GSV tributaries were found in 198 limbs (77%) at duplex scanning, of which only six (3%) resulted in recurrence. In accordance with Theivacumar et al.,¹⁵ we believe that competent GSV tributaries should not be treated as part of the primary procedure because they do not have an adverse effect on outcome 5 years after EVLA. Groin recurrence due to an incompetent anterior accessory saphenous vein can be treated easily with ultrasound-guided sclerotherapy, ambulatory phlebectomy or EVLA. Intraluminal neo-vascularisation after GSV ablation was not observed in this study. Labropoulos et al.¹⁶ identified multiple small vessels with arterial signals, directly adjacent to the involved vein segment, forming multiple small arteriovenous fistulae within the obliterated vein, which may be related to the amount of thrombus produced during EVLA and to the intensity of inflammatory response. The absence of intraluminal neo-vascularisation after GSV ablation in this study may be explained by the fact that we use manual compression over the GSV during laser energy delivery and so reduce the amount of thrombus formation.

In general, patients report high levels of satisfaction following EVLA of the GSV.¹³ In this study, VCSS scores show that during the first 6 months symptoms were significantly fewer in both groups, with no difference between groups.

In conclusion, although the rate of recurrent groin varicosities was similar, this study shows less neo-vascularisation after EVLA without SFL, but more early re-canalisation and incompetent tributaries, at 5 years' follow-up.



No (of limbs) at risk

EVLA without SFL
EVLA with SFL

43	39	33	27	14
43	42	37	28	8

Figure 3 Kaplan–Meier life table analysis of freedom from duplex-confirmed overall (Type 1a, 1b, 1c, 2a, 2b and small saphenous vein) varicose vein recurrence. EVLA, endovenous laser ablation. SFL, saphenofemoral ligation.

Limitations

The participants and the observers in the study were obviously aware of which intervention was performed due to the presence of a scar in the groin (lack of blinding). Second, to reduce the risk of bias, we selected only patients with uncomplicated C2 varicose veins and duplex-confirmed SFJ incompetence and GSV reflux from the groin to below the knee. Finally, during a 2-year period, 145 patients were considered for inclusion, of which 53 participated in the study, and, in addition, 13 patients were lost to follow-up. More cases were considered, but a longer inclusion period or a multicentre study was not possible at that time.

Acknowledgements

The authors acknowledge the contribution made by H. Janmaat for performing the Duplex ultrasound scanning during the study and thank J. Pasma for data collection and support.

Conflict of Interest/Funding

None.

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